be used for simultaneously measuring both members A and B in a binding pair complex in a biological sample by flow cytometry.

It appears that the limitation in claim 21 is not being considered because it is a label or package insert that contains printed matter. Applicant notes that the Patent and Trademark Office must consider all claim limitations when determining the patentability of an invention over the prior art. See, In re Lowry, 32 USPQ2d 1031, 1034 (Fed. Cir. 1994). As a result, proper analysis mandates that a claim be read as a whole. In re Gulack, 217 USPQ 401, 403 (Fed. Cir. 1983). Ignoring a claim element simply because the element is unpatentable by itself "is no reason for ignoring it when the claim is directed to the combination." In re Miller, 164 USPQ 46, 49 (CCPA 1969). Indeed, a patentable invention comprises a combination of all new, partly new or all old elements. Rosemount, Inc. v. Beckman Instruments, Inc., 221 USPQ 1, 7 (Fed. Cir. 1984). As dependent claim 21 further limits claim 20 by including a label or package insert, which includes instructions for use of the kit's components, the claim is proper. Applicant respectfully requests that the objection to claim 21 be withdrawn.

Rejection under 35 U.S.C. §103

The Examiner rejected claims 1-21 under 35 U.S.C. §103 as being unpatentable over O'Connor et al. (U.S. Patent No. 5,627,026) in view of Jackson et al. (U.S. Patent No. 5,776,709). The Examiner characterized the O'Connor et al. patent as disclosing "a method of detecting both members of a binding pair (antigen and antibody, for example) utilizing antibodies conjugated to different fluorescent labels." The Examiner further characterized O'Connor et al. as disclosing a method for simultaneously detecting antigen and antibody in a biological sample through the use of antibodies/antigens bound to a solid support and labeled secondary antibodies. The Examiner asserted that O'Connor et al. "differs from the claimed invention in that they do not explicitly disclose the use of flow cytometry to measure the labeled antibodies." Jackson et al. were deemed to disclose use of multiple fluorescent labels. Applicant respectfully traverses.

The combination of cited art does not teach or suggest the presently claimed invention. Independent claim 1 recites a method for simultaneously measuring both members A and B in a binding pair complex (i.e., the method is capable of detecting members A and B when bound to

each other) in a biological sample, while amended independent claim 20 recites a kit for simultaneously measuring both members A and B in a binding pair complex. The method includes:

a) providing a solid phase reagent, the solid phase reagent comprising a particle coated with capture antibodies having specific binding affinities for member A of the binding pair complex;

b) contacting the biological sample with the solid phase reagent under conditions in which member A, if present, becomes bound to the particle, to form a first reacted particle;

c) contacting the first reacted particle with first antibodies having specific binding affinities for member A, wherein the first antibodies are labeled with a first label, and with second antibodies having specific binding affinities for member B of the binding pair complex, wherein the second antibodies are labeled with a second label, to form a second reacted particle, and

d) measuring the first and second labels on the second reacted particle using flow cytometry.

The O'Connor et al. patent does not teach or suggest contacting a first reacted particle (i.e., a particle containing capture antibodies and member A, if present) with first antibodies having specific binding affinities for member A and with second antibodies having specific binding affinities for member B of the binding pair complex to form a second reacted particle, wherein the first and second antibodies include first and second labels, respectively, that are different, then measuring the first and second labels on the second reacted particle using flow cytometry. Rather, the assay of the O'Connor et al. patent uses a solid substrate that includes both antibody-coated particles and antigen-coated particles at different locations, allowing two tests (i.e., detection of antigen and detection of antibody) to be carried out simultaneously. See, for example, column 5, lines 1-9 of the O'Connor et al. patent. More particularly, the assay of the O'Connor et al. patent includes contacting a solid substrate that contains antibody-coated particles and antigen-coated particles at two different locations with a biological sample and a mixture of labeled antigen and labeled antibody. As a result, two separate immune complexes are formed, one containing substrate-bound antigen, sample antibody, and labeled antigen, and the other containing substrate-bound antibody, sample antigen, and labeled antibody. Sample

antigen and antibody are detected by determining if a label is present at the appropriate location on the solid substrate. Thus, in the assay of the O'Connor et al. patent, antigen and antibody are independently detected on two locations within a single solid phase. In contrast, the present invention allows both members of a binding pair to be detected simultaneously when the members of the binding pair are bound to each other, i.e., the members of the binding pair are detected together as a complex.

The Jackson et al. patent does not remedy the deficiencies of the O'Connor et al. patent as the Jackson et al. patent does not teach or suggest that both members of a binding pair can be measured simultaneously when bound to each other. In fact, the Jackson et al. patent does not disclose even the measurement of a binding pair. Subpopulations of leukocytes are measured with antibodies that bind to different cell surface markers. Using multiple fluorescent markers in the assay disclosed in the O'Connor et al. patent does not allow one of ordinary skill in the art to measure both members of a binding pair bound to each other in a binding pair complex. Again, the assay disclosed in the O'Connor et al. patent allows two tests to be performed simultaneously such that antigen and antibody are independently detected on a single solid substrate. As the combination of the cited patents does not teach the simultaneous measurement of both members of a binding pair in a complex, Applicant submits that the present claims are non-obvious. The Examiner is respectfully requested to withdraw the rejection of claims 1-21 under 35 U.S.C. §103.

CONCLUSION

Applicant asks that claims 1-21 be allowed. The Examiner is invited to telephone the undersigned agent if it is felt that such would advance prosecution of the application.

No fees are believed due as this response is being filed before the end of the shortened statutory period. Please apply any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 8/16/01

Monica McCormick Graham, Ph.D.
Reg. No. 42,600

Fish & Richardson P.C., P.A.
60 South Sixth Street
Suite 3300
Minneapolis, MN 55402
Telephone: (612) 335-5070
Facsimile: (612) 288-9696

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